WEST Search History

DATE: Wednesday, September 10, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L13	l10 and mytilus	6	L13
L12	L10 and defensin	5	L12
L11	L10 and mytilins	0	L11
L10	antimicrobial and mollusc	185	L10
L9	myticin	1	L9
L8	L5 and mollusc	1	L8
L7	L5 and myticin	1	L7
L6	L5 and antimicrobial	1	L6
L5	l1 or l2 or l3 or l4	40	L5
L4	noel-thierry.in.	34	L4
L3	hubert-florence.in.	1	L3
L2	mitta-guillaume.in.	1	L2
L1	roch-philippe.in.	7	L1

END OF SEARCH HISTORY

10/030231

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NEWS 25	Jul 16	Data from 1960-1976 added to RDISCLOSURE
NEWS 26	Jul 21	Identification of STN records implemented
NEWS 27	Jul 21	Polymer class term count added to REGISTRY
NEWS 28	Jul 22	INPADOC: Basic index (/BI) enhanced; Simultaneous Left and Right Truncation available
NEWS 29	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS 30	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS 31	AUG 15	PATDPAFULL: one FREE connect hour, per account, in September 2003
NEWS 32	AUG 15	PCTGEN: one FREE connect hour, per account, in September 2003
NEWS 33	AUG 15	RDISCLOSURE: one FREE connect hour, per account, in September 2003
NEWS 34	AUG 15	TEMA: one FREE connect hour, per account, in September 2003
NEWS 35	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS 36	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS 37	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Right Truncation
NEWS 38	AUG 18	Simultaneous left and right truncation added to ANABSTR

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               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> e roch philippe/au
E1            3     ROCH PETR/AU
E2           11     ROCH PH/AU
E3           75 --> ROCH PHILIPPE/AU
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E6           31     ROCH R/AU
E7            5     ROCH R H/AU
E8            2     ROCH R R/AU
E9            1     ROCH RAINALD/AU
E10           1     ROCH RAME F/AU
E11         323     ROCH RAMEL F/AU
E12          84     ROCH RAMEL FRANCOISE/AU

=> s e3
L1           75 "ROCH PHILIPPE"/AU

=> e mitta guillaume/au
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E3           19 --> MITTA GUILLAUME/AU
E4            1     MITTA ISAMU/AU
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E8            1     MITTA KENRO/AU
E9           68     MITTA M/AU
E10           2     MITTA M L/AU
E11           1     MITTA M M/AU
E12          31     MITTA MASANORI/AU

=> s e2-e3
L2           56 ("MITTA G"/AU OR "MITTA GUILLAUME"/AU)

=> e hubert florence/au
E1            1     HUBERT FERRARI A/AU
E2            1     HUBERT FERRARI AURELLA/AU
E3           17 --> HUBERT FLORENCE/AU
E4            1     HUBERT FOUCHARD I/AU
E5            1     HUBERT FRANCIS/AU
E6            4     HUBERT FRANCK/AU
E7           13     HUBERT FRANCOIS/AU
E8            3     HUBERT FRANCOIS XAVIER/AU
E9            2     HUBERT FRANCOISE/AU
E10           1     HUBERT FRANZ/AU
E11           3     HUBERT FRANZ E/AU
E12           2     HUBERT FRED JR/AU

=> s e3
L3           17 "HUBERT FLORENCE"/AU

=> e noel thierry/au
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E5           30     NOEL TIMOTHY R/AU
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E12           2     NOEL VIRGINIE/AU

=> s e3
L4           27 "NOEL THIERRY"/AU
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=> s l1-l4
L5          134 (L1 OR L2 OR L3 OR L4)

=> s l5 and myticin
L6           13 L5 AND MYTICIN

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7             5 DUP REM L6 (8 DUPLICATES REMOVED)

=> d bib ab 1-5

L7   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
AN   2001:50800  CAPLUS
DN   134:111262
TI   Mytilus myticins and cDNAs, their production with recombinant cells, and
     their use as antimicrobial agents
IN   Roch, Philippe; Mitta, Guillaume; Hubert,
     Florence; Noel, Thierry
PA   Centre National de la Recherche Scientifique (CNRS), Fr.; Institut
     Francais de Recherche pour l'Exploitationde La Mer (IFREMER)
SO   PCT Int. Appl., 24 pp.
     CODEN: PIXXD2
DT   Patent
LA   French
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
     ---------------    ----  --------       ---------------   --------
PI   WO 2001004294      A1    20010118       WO 2000-FR1975    20000707
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     FR 2796072          A1    20010112       FR 1999-8858      19990708
     EP 1194550          A1    20020410       EP 2000-949681    20000707
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2003504055       T2    20030204       JP 2001-509498    20000707
PRAI FR 1999-8858        A     19990708
     WO 2000-FR1975      W     20000707
AB   The invention concerns an antimicrobial peptide, called myticin,
     characterized in that it can be obtained from a bivalve mollusc shellfish,
     and its mol. mass is about 4.5 kDa; its pI is about 8.7; it comprises 8
     cysteines. The invention also concerns its prepn. and its uses. The
     invention further concerns a nucleic acid coding for said peptide. Thus,
     myticins a and b were purified from Mytilus galloprovincialis and their
     antibacterial, antifungal, and antiprotozoal activities examd. Addnl.,
     the cDNAs encoding the prepromyticins were cloned and sequenced.
RE.CNT  5    THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 2 OF 5  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
     DUPLICATE 1
AN   2000:440517  BIOSIS
DN   PREV200000440517
TI   Differential distribution and defence involvement of antimicrobial
     peptides in mussel.
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PA CNRS; IFREMER
LO France.
PI FR 2796072 21 Jan 2001
AI FR 1999-8858 8 Jul 1999
PRAI FR 1999-8858 8 Jul 1999
DT Patent
LA French
OS WPI: 2001-149782 [16]
AB New antibiotic peptides (I), myticines, obtainable from a bivalve mollusc, have a mol. wt. of about 4,500, have an isoelectric point of about 8.7 and comprise 8 cysteine residues. Also claimed are: a nucleic acid (II) comprising a sequence encoding (I); an oligonucleotide comprising a segment of at least 15 bp; an expression cassette comprising (II) under the transcriptional control of a promoter; a recombinant vector ; a prokaryotic or eukaryotic cell transformed with (II); and production of (I) by expression of (II) in the cell. (I) have antibacterial and fungicidal activity and can be used to prepare anti-infective medicaments and to prevent and treat microbial diseases in various sectors, e.g. health, agriculture, aquaculture and animal husbandry. (18pp)

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:50800 CAPLUS
DN 134:111262
TI Mytilus myticins and cDNAs, their production with recombinant cells, and their use as antimicrobial agents
IN **Roch, Philippe; Mitta, Guillaume; Hubert, Florence; Noel, Thierry**
PA Centre National de la Recherche Scientifique (CNRS), Fr.; Institut Francais de Recherche pour l'Exploitationde La Mer (IFREMER)
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004294	A1	20010118	WO 2000-FR1975	20000707
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2796072	A1	20010112	FR 1999-8858	19990708
	EP 1194550	A1	20020410	EP 2000-949681	20000707
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003504055	T2	20030204	JP 2001-509498	20000707
PRAI	FR 1999-8858	A	19990708		
	WO 2000-FR1975	W	20000707		

AB The invention concerns an **antimicrobial peptide**, called myticin, characterized in that it can be obtained from a bivalve mollusc shellfish, and its mol. mass is about 4.5 kDa; its pI is about 8.7; it comprises 8 cysteines. The invention also concerns its prepn. and its uses. The invention further concerns a nucleic acid coding for said peptide. Thus, myticins a and b were purified from Mytilus galloprovincialis and their antibacterial, antifungal, and antiprotozoal activities examd. Addnl., the cDNAs encoding the prepromyticins were cloned and sequenced.

The results show that the expression of both mytilin B and MGD2 is developmentally regulated, but neither gene is expressed in mussels until after larval settlement and metamorphosis. Finally, the genes encoding two isoforms of these peptides have been cloned and sequenced, revealing that both genes contain four exons and three introns.

L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:895883 CAPLUS
DN 134:221056
TI Original involvement of antimicrobial peptides in mussel innate immunity
AU **Mitta, G.**; Vandenbulcke, F.; Roch, P.
CS Defense et Resistance chez les Invertebres Marins (DRIM), UMR 5098, Universite de Montpellier 2, Montpellier, 34095, Fr.
SO FEBS Letters (2000), 486(3), 185-190
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal; General Review
LA English
AB A review with 37 refs. Recently, the existence and extended diversity of antimicrobial peptides has been revealed in two mussel species. These mols. are classified into four groups according to common features of their primary structure: defensins, mytilins, myticins and mytimycin. In Mytilus galloprovincialis, gene structure reveals synthesis as precursors in circulating hemocytes. Synthesized even in absence of challenge, the precursors mature and the peptides are stored in granules as active forms. The different peptides are engaged in the destruction of bacteria inside phagocytes, before being released into hemolymph to participate in systemic responses. Such involvement in anti-infectious responses is unique, and apparently more related to those of mammalian phagocytes than to those of insects.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:377518 BIOSIS
DN PREV200000377518
TI A new model of involvement of antimicrobial peptides in invertebrates.
AU **Mitta, Guillaume (1)**; Vandenbulcke, Franck (1); Salzet, Michel (1); **Roch, Philippe**
CS (1) Centre de Biologie Cellulaire, Laboratoire d'Endocrinologie des Annelides, Groupe de Neuro-immunite des Hirudinees, Universite des Sciences et Techniques de Lille, Lille France
SO Developmental & Comparative Immunology, (2000) Vol. 24, No. Supplement 1, pp. S20. print.
Meeting Info.: 8th Congress of the International Society of Developmental and Comparative Immunology Cairns, Australia July 03-06, 2000
ISSN: 0145-305X.
DT Conference
LA English
SL English

L9 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 1999:483780 BIOSIS
DN PREV199900483780
TI Myticin, a novel cysteine-rich **antimicrobial peptide** isolated from haemocytes and plasma of the mussel Mytilus galloprovincialis.
AU **Mitta, Guillaume; Hubert, Florence; Noel, Thierry; Roch, Philippe (1)**
CS (1) UMR 219 DRIM, Universite de Montpellier 2, place Eugene Bataillon, F-34095, Montpellier France
SO European Journal of Biochemistry, (Oct., 1999) Vol. 265, No. 1, pp. 71-78.

ISSN: 0014-2956.
DT Article
LA English
SL English
AB We report here the isolation of two isoforms of a novel cysteine-rich peptide from haemocytes (isoform A of 4.438 Da and B of 4.562 Da) and plasma (isoform A) of the mussel, Mytilus galloprovincialis. The two molecules display antibacterial activity against gram-positive bacteria, whereas only isoform B is active against the fungus Fusarium oxysporum and a gram-negative bacteria Escherichia coli D31. Complete peptide sequences were determined by a combination of Edman degradation, mass spectrometry and cDNA cloning using a haemocyte cDNA library. The mature molecules, named myticins, comprise 40 residues with four intramolecular disulfide bridges and a cysteine array in the primary structure different to that of the previously characterized cysteine-rich antimicrobial peptides. Sequence analysis of the cloned cDNAs revealed that myticin precursors consist of 96 amino acids with a putative signal peptide of 20 amino acids, the **antimicrobial peptide** sequence and a 36-residue C-terminal extension. This structure suggests that myticins are synthesized as preproproteins and then processed by various proteolytic events before storage of the active peptide in the haemocytes. Myticin precursors are expressed mainly in the haemocytes as revealed by Northern blot analysis.

L9 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 1998:206080 BIOSIS
DN PREV199800206080
TI Solution structure of the **antimicrobial peptide** ranalexin and a study of its interaction with perdeuterated dodecylphosphocholine micelles.
AU Vignal, Emmanuel; Chavanieu, Alain; **Roch, Philippe**; Chiche, Laurent; Grassy, Gerard; Calas, Bernard; Aumelas, Andre (1)
CS (1) Cent. Biochim. Structurale, UMR 9955, U414 INSERM, Fac. Pharmacie, 15 avenue Charles Flahault, F-34060 Montpellier Cedex 2 France
SO European Journal of Biochemistry, (April, 1998) Vol. 253, No. 1, pp. 221-228.
ISSN: 0014-2956.
DT Article
LA English
AB Ranalexin, a 20-residue peptide isolated from the skin of the bullfrog Rana catesbeiana displays antimicrobial activity. This peptide contains two cysteine residues in positions 14 and 20 linked by a disulphide bridge. Ranalexin was chemically synthesized and close antimicrobial activities were measured for the reduced and oxidized forms. The solution structure of ranalexin was determined by using circular dichroism, proton NMR spectroscopy and molecular modelling techniques. The reduced and oxidized forms of ranalexin are mainly unstructured in water but display an alpha-helical structure spanning residues 8-15 and 8-17, respectively, in a trifluoroethanol/water mixture (3:7, by vol.). Ranalexin was found to interact with micelles of dodecylphosphocholine and to adopt a similar helical structure. Moreover, slow-exchanging amide protons located on the same side of the helix suggest that the hydrophobic face of the helix lies on the micelle surface. Hydrophobic residues of the poorly structured N-terminal part which are important for the biological activity are also involved in the interaction with micelles. Taken together, the results suggest that the disulphide bond does not strongly affect either the conformation or the antimicrobial activity of ranalexin.

=> s antimicrobial and (mollusc? or mussel)
L10 398 ANTIMICROBIAL AND (MOLLUSC? OR MUSSEL)

=> s l10 and mytilus
L11 68 L10 AND MYTILUS

=> s l11 and (protein or peptid?)
L12 54 L11 AND (PROTEIN OR PEPTID?)

=> dup rem l12
PROCESSING COMPLETED FOR L12
L13 20 DUP REM L12 (34 DUPLICATES REMOVED)

=> d bib ab 1-20

L13 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:536528 CAPLUS
DN 139:115939
TI Progress of research on **mussel** defensins
AU Chen, Haowen; Wei, Yuxi; Guo, Daosen
CS First Institute of Oceanography, SOA, Shandong, 266061, Peop. Rep. China
SO Guangxi Kexue (2003), 10(2), 129-134
CODEN: GKUEAC; ISSN: 1005-9164
PB Guangxi Kexue Bianjibu
DT Journal; General Review
LA Chinese
AB A review. Defensins contained in **mussel** and other marine **mollusca** are important **antimicrobial peptides**. The **mussel** defensins known update are divided into four groups according to character, primary structure and mutual cysteine sequence. They are **mytilus** defensins (MDA and MDB), **Mytilus** gallovoprovincial defensins (MGD1 and MGD2); Myticins A and B; Mytilins A, B, C, D, G1; and Mytimycin. Their chem. character and structure, prodn. and bioactivities are explained. The mussels living in various environments are not subjected to serious diseases, and resist invading of diverse pathogens and protect themselves from enemy microbials. The research on **mussel** defensins contribute to ou understanding of innate immunity of mussels and other marine mollusks, and in improvement of maricultural techniques.

L13 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:679462 CAPLUS
DN 137:309312
TI Bacterial killing by **Mytilus** hemocyte monolayers as a model for investigating the signaling pathways involved in **mussel** immune defence
AU Canesi, L.; Scarpato, A.; Betti, M.; Ciacci, C.; Pruzzo, C.; Gallo, G.
CS Istituto di Scienze Fisiologiche, Universita di Urbino, Urbino (PS), 61029, Italy
SO Marine Environmental Research (2002), 54(3-5), 547-551
CODEN: MERSDW; ISSN: 0141-1136
PB Elsevier Science Ltd.
DT Journal
LA English
AB The signaling pathways involved in **mussel** immune defense were investigated utilizing a model of killing of Escherichia coli by **Mytilus** galloprovincialis hemocytes in a co-culture setting. In particular, the role played by different mitogen activated **protein** kinases (MAPKs) and by the prodn. of eicosanoids were investigated utilizing specific cell permeant, pharmacol. enzyme inhibitors. Hemocyte pretreatment with the p38 MAPK inhibitor SB203580 significantly reduced bacterial killing, whereas PD98059 (an inhibitor of ERK-extracellularly regulated kinase-MAPK activation) had no significant effect. Wortmannin also inhibited bacterial killing, indicating a crucial role for PI3-kinase activation in the immune response. Killing of E. coli was also reduced by inhibitors of both PLA2 and cyclooxygenase activities, indicating that

eicosanoid prodn. is involved in mediating the response to bacterial challenge. The results demonstrate that bacterial killing by **mussel** hemocytes is particularly sensitive to inhibitors of the key steps involved in the transduction of bacterial signals into the host cell. Moreover, these data indicate that the hemocyte bactericidal activity can be suitably utilized not only for identifying the signaling pathways involved in the response to bacterial infection, but also as a potential investigative-toxicol. model to test drugs and contaminants for their effect on the overall **mussel** immune defense.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:923038 CAPLUS
DN 138:121563
TI Behaviour of defense **peptides** in environmentally stressed mussels
AU Roch, Ph.
CS Defense et Resistance chez les Invertebres Marins, UMR 5098 IFREMER-CNRS-Universite de Montpellier 2, Fr.
SO Revue de Medecine Veterinaire (Toulouse, France) (2002), 153(7), 517-520 CODEN: RVMVAH; ISSN: 0035-1555
PB Ecole Nationale Veterinaire de Toulouse
DT Journal
LA English
AB Few data concern the effect of environmental stressors upon the regulation of anti infectious functions in **molluscs**. In mussels, the immune system includes **antimicrobial peptides** (defensins, mytilins and myticins) which are stored in hemocyte granules and released upon activation by bacterial challenge. We report here on the effects of bacteria, heat-shock and PAH (phenanthrene) on **antimicrobial** gene expression in hemocytes using mol. biol. approaches. In mussels collected in early summer (June), defensin expression was almost undetectable, but both mytilin and myticin mRNAs were present. In opposing circumstances where mussels were collected in winter (Feb.), basic level of defensin expression was already high. Immediately after heat-shock, no significant change in hybridization intensity was obsd. for both mytilin and myticin. In summer, defensin showed a marked increase in expression, gradually returning to virtually no expression 24 h after. In winter, defensin expression was maintained during 30 min, then dramatically decreased to become almost undetectable even after 9 h under stress. Consequently, only defensin gene expression appears to be modulated by elevated temps. This has to be confronted with reported summer mortality, a multifactorial process, which depends on the temp. effect on the balance between pathogen and immune capabilities. Hydrocarbon contamination is common in the marine environment and involves many components, including highly toxic PAHs. Mussels were exposed in the lab. for 7 days to phenanthrene concns. ranging from 50 to 400 ppb. This expt. was done in Feb., at the time defensin genes were expressed. No modification of the quantities of mytilin and myticin mRNAs was detected in hemocytes, suggesting that expression of the corresponding genes was not modified by such contaminant exposure. In contrast, the relative level of defensin was depressed from the lowest dose of 50 ppb upwards. Here also, defensin genes display different behavior from mytilin and myticin counterparts. The biol. significance of such a phenomenon might be related to specificity of the various **peptides** in relationship with bacteria present in the environment.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 1
AN 2001-149782 [16] WPIDS
DNC C2001-044468

TI New **antimicrobial peptides** myticines obtainable from a bivalve **mollusc**, especially **Mytilus** galloprovincialis are useful for treatment and prevention of microbial disease.
DC B04 D16
IN HUBERT, F; MITTA, G; NOEL, T; ROCH, P
PA (CNRS) CNRS CENT NAT RECH SCI; (IFRE-N) IFREMER INST FR RECH EXPL MER; (FRRE-N) INST FR RECH EXPL MER
CYC 95
PI FR 2796072 A1 20010112 (200116)* 18p
WO 2001004294 A1 20010118 (200116) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000062962 A 20010130 (200127)
EP 1194550 A1 20020410 (200232) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003504055 W 20030204 (200320) 23p
ADT FR 2796072 A1 FR 1999-8858 19990708; WO 2001004294 A1 WO 2000-FR1975 20000707; AU 2000062962 A AU 2000-62962 20000707; EP 1194550 A1 EP 2000-949681 20000707, WO 2000-FR1975 20000707; JP 2003504055 W WO 2000-FR1975 20000707, JP 2001-509498 20000707
FDT AU 2000062962 A Based on WO 2001004294; EP 1194550 A1 Based on WO 2001004294; JP 2003504055 W Based on WO 2001004294
PRAI FR 1999-8858 19990708
AB FR 2796072 A UPAB: 20010323
NOVELTY - New **antimicrobial peptides** (I), myticines, obtainable from a bivalve **mollusc**, have a molecular weight of about 4.5 kD, have an isoelectric point of about 8.7 and comprise 8 cysteine residues.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid (II) comprising a sequence encoding (I);

(2) an oligonucleotide comprising a segment of at least 15 base pairs (bp) of the nucleic acid of (1);

(3) an expression cassette comprising (II) under the transcriptional control of a promoter;

(4) a recombinant vector comprising (II);

(5) a prokaryotic or eukaryotic cell transformed with (II);

(6) production of (I) by expression of (II) in the cell of (5).

ACTIVITY - **Antimicrobial**; antibacterial; fungicidal.

Myticine a had a minimum bactericidal concentration of 2.25-4.5 against Micrococcus luteus and Bacillus megaterium and 4.5-9 against Aerococcus viridans and was inactive against other Gram-positive and -negative bacteria tested and against Fusarium oxysporum and the oyster parasite Perkinsus marinus.

MECHANISM OF ACTION - None given.

USE - (I) have antibacterial and fungicidal activity and can be used to prepare anti-infective medicaments and to prevent and treat microbial diseases in various sectors, e.g. health, agriculture, aquaculture and animal husbandry.

Dwg.0/0

L13 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:50800 CAPLUS
DN 134:111262
TI **Mytilus** myticins and cDNAs, their production with recombinant cells, and their use as **antimicrobial** agents
IN Roch, Philippe; Mitta, Guillaume; Hubert, Florence; Noel, Thierry
PA Centre National de la Recherche Scientifique (CNRS), Fr.; Institut

Francais de Recherche pour l'Exploitationde La Mer (IFREMER)
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001004294	A1	20010118	WO 2000-FR1975	20000707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2796072	A1	20010112	FR 1999-8858	19990708
EP 1194550	A1	20020410	EP 2000-949681	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003504055	T2	20030204	JP 2001-509498	20000707
PRAI FR 1999-8858	A	19990708		
WO 2000-FR1975	W	20000707		

AB The invention concerns an **antimicrobial peptide**, called myticin, characterized in that it can be obtained from a bivalve **mollusc** shellfish, and its mol. mass is about 4.5 kDa; its pI is about 8.7; it comprises 8 cysteines. The invention also concerns its prepn. and its uses. The invention further concerns a nucleic acid coding for said **peptide**. Thus, myticins a and b were purified from **Mytilus** galloprovincialis and their antibacterial, antifungal, and antiprotozoal activities examd. Addnl., the cDNAs encoding the prepromyticins were cloned and sequenced.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2002:205350 BIOSIS
DN PREV200200205350
TI A comparative study of anti-Perkinsus marinus activity in bivalve sera.
AU Anderson, Robert S. (1); Beaven, Amy E. (1)
CS (1) Chesapeake Biological Laboratory, University of Maryland Center for Environmental Science, Solomons, MD, 20688 USA
SO Journal of Shellfish Research, (December, 2001) Vol. 20, No. 3, pp. 1011-1017. print.
ISSN: 0730-8000.
DT Article
LA English
AB The eastern oyster Crassostrea virginica has been decimated by a protistan parasite Perkinsus marinus; however, other bivalves appear to be more resistant to this pathogen. To better understand the basis for this difference in susceptibility, a comparative study of the activities of anti-P. marinus serum proteins of several bivalve species was carried out. Sera from mussels not known to develop P. marinus disease, **Mytilus** edulis and Geukensia demissa, contained high and-P. marinus activity. About 25% of M. edulis serum samples contained <10 kDa anti-P. marinus **peptides**; the possibility of seasonal, geographic, or other reasons to explain this variability requires additional study. Anti-P. marinus **peptides** in G. demissa serum were apparently absent. Measurable anti-P. marinus activity was present in C. virginica and C. gigas sera, but at levels many hundred-fold lower than that of the

mussels. The greater P. marinus resistance of C. gigas vs. C. virginica could not be explained by differences in anti-P. marinus activity of their sera. Hemocyte lysates from all the bivalves examined produced marked inhibition of the growth of P. marinus, suggesting that **antimicrobial** agents may be secreted by hemocytes into the serum. These factors may also participate in intracellular destruction of P. marinus, since the killing ability of the hemocytes of the different species closely mirrored the anti-P. marinus activities of their sera. The data suggest that C. virginica lacks active anti-P. marinus serum agents typical of M. edulis and G. demissa; however, P. marinus resistance of C. gigas seems not to depend upon elevated levels of **antimicrobial** serum factors.

L13 ANSWER 7 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2002:117723 BIOSIS
DN PREV200200117723
TI Antibacterial activities of oyster (Crassostrea virginica) and **mussel** (**Mytilus** edulis and Geukensia demissa) plasma.
AU Anderson, Robert S. (1); Beaven, Amy E.
CS (1) Chesapeake Biological Laboratory, University of Maryland Center for Environmental Science, Solomons, MD, 20688: anderson@cbl.umces.edu USA
SO Aquatic Living Resources, (November December, 2001) Vol. 14, No. 6, pp. 343-349. print.
ISSN: 0990-7440.
DT Article
LA English
AB Anti-Bacillus megaterium activity was measured in unfractionated plasma withdrawn from three common US East Coast bivalve **molluscs**: an oyster Crassostrea virginica and the mussels Geukensia demissa and **Mytilus** edulis. The activities of the plasma samples from these bivalves were also measured against a C. virginica pathogen Perkinsus marinus. Strong anti-B. megaterium activity was measured in plasma from C. virginica and M. edulis, but was not detected in G. demissa. Bactericidal activity was found in hemocyte extracts from all bivalves in this study, suggesting a cellular origin of cytotoxic humoral factors. **Peptides** (< 10 kDa) were separated from the plasma samples by ultrafiltration; weak antibacterial **peptide** activity was quantified in C. virginica **peptides**, but not in **peptides** from the mussels. In the case of P. marinus, plasma from M. edulis or G. demissa was strongly cidal as compared to plasma from C. virginica. This difference in activity probably reflects the low pathogenicity of this oyster parasite for the **mussel** species tested. In summary, the bactericidal activity of plasma proteins from these bivalves showed considerable interspecies variation and did not necessarily correlate directly with antiprotistan activity. When present, antibacterial and antiprotistan activities seemed to be associated with plasma proteins rather than < 10-kDa plasma **peptides**, with the possible exception of C. virginica anti-B. megaterium activity and the occasionally expressed anti-P. marinus activity of M. edulis **peptides**. The precise identity of the plasma **protein**(s) responsible for the **antimicrobial** activities measured have yet to be determined, but it is likely that agents other than, or in addition to, lysozyme play significant roles in the process.

L13 ANSWER 8 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4
AN 2002:175305 BIOSIS
DN PREV200200175305
TI Solution structure and activity of the synthetic four-disulfide bond Mediterranean **mussel** defensin (MGD-1.
AU Yang, Yin-Shan; Mitta, Guillaume; Chavanieu, Alain; Calas, Bernard; Sanchez, Jean Frederic; Roch, Philippe; Aumelas, Andre (1)

hemocyte cDNA library. This precursor contains a putative signal **peptide** of 22 residues, a processing **peptide** sequence of 34 amino acids, and a C-terminal extension of 48 residues rich in acidic residues. Distribution of mytilin B mRNA and of the corresponding **peptide** in various **mussel** tissues revealed that mytilins are synthesized and stored in a specific hemocyte subtype. Furthermore, in an experimental model of infection, we showed (i) a recruitment of hemocytes containing mytilins toward the injection site within hours following bacterial challenge, (ii) that mytilins probably play a prominent role in killing intracellular bacteria after phagocytosis, and (ii) later an increase of mytilin-like material occurred in the plasma suggesting a secondary systemic role.

L13 ANSWER 10 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
AN 2000:440517 BIOSIS
DN PREV200000440517
TI Differential distribution and defence involvement of **antimicrobial peptides** in **mussel**.
AU Mitta, Guillaume; Vandenbulcke, Franck; Noel, Thierry; Romestand, Bernard; Beauvillain, Jean Claude; Salzet, Michel; Roch, Philippe (1)
CS (1) Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER-CNRS-Universite de Montpellier 2, 34095, Montpellier France
SO Journal of Cell Science, (August, 2000) Vol. 113, No. 15, pp. 2759-2769. print.
ISSN: 0021-9533.
DT Article
LA English
SL English
AB In previous papers, we characterised 3 types of 4-kDa, cysteine-rich, cationic **antimicrobial peptides**: MGDs (for **Mytilus** galloprovincialis defensins), mytilins and myticins, which are abundant in the **mussel** hemocytes. In the present work, we revealed a differential distribution of the cells expressing the different genes. In addition, using confocal and electron microscopy, we confirmed that defensins and mytilins were partially located in different sub-types of circulating hemocytes although the **peptides** can be located in the same cell, and even in the same granule. We also demonstrated that mytilins exert their microbicidal effect within the cells through the process of phagosome-mytilin granule fusion leading to the co-location of ingested bacteria and mytilins.

L13 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:337078 CAPLUS
DN 133:88077
TI Immunomodulation by recombinant human interleukin-8 and its signal transduction pathways in invertebrate hemocytes
AU Ottaviani, E.; Franchini, A.; Malagoli, D.; Genedani, S.
CS Department of Animal Biology, University of Modena and Reggio Emilia, Modena, I-41100, Italy
SO Cellular and Molecular Life Sciences (2000), 57(3), 506-513
CODEN: CMLSFI; ISSN: 1420-682X
PB Birkhaeuser Verlag
DT Journal
LA English
AB We report the presence of interleukin (IL)-8-immunoreactive mols. in hemocytes from the **mollusc Mytilus** galloprovincialis. Functional studies demonstrate that recombinant human (rh)IL-8 provokes conformational changes, induces chemotaxis, and increases bacterial phagocytic activity in hemocytes. RhIL-8 induces cell shape changes via **protein** kinase A and C pathways. These morphol. changes are followed by reorganization of the actin microfilaments. The findings suggest that, as previously reported for other cytokines, IL-8 is well

conserved and deeply involved in immune functions from invertebrates to mammals.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7
AN 2000:241254 BIOSIS
DN PREV200000241254
TI Mytilin B and MGD2, two **antimicrobial peptides** of marine mussels: Gene structure and expression analysis.
AU Mitta, Guillaume; Hubert, Florence; Dyrynda, Elisabeth A.; Boudry, Pierre; Roch, Philippe (1)
CS (1) UMR 219 Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER/CNRS Universite de Montpellier 2, Universite de Montpellier 2, CC 80, 34095, Montpellier France
SO Developmental & Comparative Immunology, (June, 2000) Vol. 24, No. 4, pp. 381-393.
ISSN: 0145-305X.
DT Article
LA English
SL English
AB Previous research has shown that mytilins and MGDs are two types of 4-kDa, cysteine-rich, cationic **antimicrobial peptides**, which are abundant in hemocytes of the mussels, **Mytilus** galloprovincialis and M. edulis. The expression of the genes encoding these **peptides** has been analyzed in the hemocytes of animals subjected to various stress factors, as well as during larval development. Variations in gene expression in adult mussels have been tested under conditions of physical stress, bacterial challenge and heat shock. The results suggest that in adult mussels, the MGD2 gene may be over-expressed with physical and temperature stress, but that reduced expression occurs with bacterial challenge. Gene expression during development has been analyzed using different larval and post-larval stages, ranging from 4-day-old veliger larvae to 32-day-old post-larvae. The results show that the expression of both mytilin B and MGD2 is developmentally regulated, but neither gene is expressed in mussels until after larval settlement and metamorphosis. Finally, the genes encoding two isoforms of these **peptides** have been cloned and sequenced, revealing that both genes contain four exons and three introns.

L13 ANSWER 13 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
AN 2001:187667 BIOSIS
DN PREV200100187667
TI Original involvement of **antimicrobial peptides** in **mussel** innate immunity.
AU Mitta, Guillaume; Vandenbulcke, Franck; Roch, Philippe (1)
CS (1) Defense et Resistance chez les Invertebres Marins (DRIM), UMR 5098, Universite de Montpellier 2, Place E. Bataillon, 34095, Montpellier: proch@ifremer.fr France
SO FEBS Letters, (15 December, 2000) Vol. 486, No. 3, pp. 185-190. print.
ISSN: 0014-5793.
DT General Review
LA English
SL English
AB Recently, the existence and extended diversity of **antimicrobial peptides** has been revealed in two **mussel** species. These molecules are classified into four groups according to common features of their primary structure: defensins, mytilins, myticins and mytimycin. In **Mytilus** galloprovincialis, gene structure reveals synthesis as precursors in circulating hemocytes. Synthesised even in absence of challenge, the precursors mature and the **peptides** are stored in

granules as active forms. The different **peptides** are engaged in the destruction of bacteria inside phagocytes, before being released into hemolymph to participate in systemic responses. Such involvement in anti-infectious responses is unique, and apparently more related to those of mammalian phagocytes than to those of insects.

L13 ANSWER 14 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:377518 BIOSIS
DN PREV200000377518
TI A new model of involvement of **antimicrobial peptides** in invertebrates.
AU Mitta, Guillaume (1); Vandenbulcke, Franck (1); Salzet, Michel (1); Roch, Philippe
CS (1) Centre de Biologie Cellulaire, Laboratoire d'Endocrinologie des Annelides, Groupe de Neuro-immunite des Hirudinees, Universite des Sciences et Techniques de Lille, Lille France
SO Developmental & Comparative Immunology, (2000) Vol. 24, No. Supplement 1, pp. S20. print.
Meeting Info.: 8th Congress of the International Society of Developmental and Comparative Immunology Cairns, Australia July 03-06, 2000
ISSN: 0145-305X.
DT Conference
LA English
SL English

L13 ANSWER 15 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 9
AN 1999-312395 [26] WPIDS
DNC C1999-092172
TI **Antimicrobial** composition containing active **protein** isolated from mussels and carbohydrates, used for cleaning contaminated tissues or treating wounds.
DC B04 B07 D22
IN DE FAIRE, J
PA (MICR-N) MICRO ACTIVE PROTEIN IN SWEDEN AB
CYC 82
PI WO 9909835 A1 19990304 (199926)* EN 14p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9888950 A 19990316 (199930)
ADT WO 9909835 A1 WO 1998-SE1510 19980824; AU 9888950 A AU 1998-88950 19980824
FDT AU 9888950 A Based on WO 9909835
PRAI SE 1997-3085 19970827
AB WO 9909835 A UPAB: 19990707
NOVELTY - The use of a composition containing at least one antimicrobially active **protein** (I), isolated from mussels and carbohydrates, is claimed in a product having **antimicrobial** activity and coagulant effect, for:
(a) treating and cleaning microbially contaminated tissues, body surfaces or cavities, and/or
(b) treating bleeding wounds, lesions and damaged tissues.
ACTIVITY - Antibacterial; coagulant. Test samples were prepared by dissolving lyophilized powder comprising active **protein** isolated from **Mytilus** edulis in 0.9% saline ((A) 0.005, (B) 0.05 or (C) 0.5 mu g/ml). Test samples or saline (20 mu l) were added to fresh blood (200 mu l) on glass slides. The slides were held vertically every 15 seconds, and time to clotting determined. Results for clotting times (seconds) were: (A) 120, (B) 90 and (C) 90, compared with 195 for the saline control and 165 for blood alone.
MECHANISM OF ACTION - None given.

USE - The product is for external use, e.g. as an adhesive dressing, a band aid, bandage or dressing; or for internal use, e.g. as a suture thread, catheter or an implant (optionally biodegradable). Such products improve blood coagulation and prevent tissue adhesion.

ADVANTAGE - Use of the composition results in decreased bleeding time of bleeding wounds and improved tissue healing.

L13 ANSWER 16 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 10
AN 1999-204405 [17] WPIDS
DNN N1999-150581 DNC C1999-059468
TI Purification of fluidising **antimicrobial** composition in combination with chemical or physical filter - where **antimicrobial** composition contains **protein** isolated form mussels.
DC C05 D15 D22 P34
IN DE FAIRE, J
PA (MICR-N) MICRO ACTIVE PROTEIN IN SWEDEN AB
CYC 82
PI WO 9908535 A1 19990225 (199917)* EN 20p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
SE 9702993 A 19990219 (199919)
AU 9887547 A 19990308 (199929)
ADT WO 9908535 A1 WO 1998-SE1466 19980813; SE 9702993 A SE 1997-2993 19970818; AU 9887547 A AU 1998-87547 19980813
FDT AU 9887547 A Based on WO 9908535
PRAI SE 1997-2993 19970818
AB WO 9908535 A UPAB: 19990503
NOVELTY - Purification of fluidising **antimicrobial** composition containing a **protein** isolated form mussels, in combination with a chemical or physical filter. DETAILED DESCRIPTION - Purification of fluid comprises treating the fluid using an **antimicrobial** composition containing an antimicrobially active **protein** (I), isolated from mussels and carbohydrates such as glycogen, where the method further comprises treating the fluid using at least one chemical/physical filter or process with the capability of removing particles or compounds dissolved or suspended in the fluid.

USE - The method is used for purification of water from contaminating micro-organisms, viruses, toxins and particles and compounds causing bad taste odour, discoloration and turbidity. The method is useful for purification of water, including drinking water, form contaminating micro-organisms, viruses, toxins and particles causing bad taste, odor, discoloration and turbidity. Surface water from a river was collected up-town Uppsala, Sweden, in a rural area at the end of April (year not specified). The water was diluted 100-fold with autoclaved water and cultured for heterotrophic microbes, coliform microbes and E. Coli and microfungi. 0.1 mg Lyophilised powder containing an extract of **Mytilus** edulis, active **protein** having a molecular weight of 18-20 kda with a possible dimeric form at 35-38 kda by SDS-PAGE electrophoresis, and comprising 3-4% carbohydrates, mainly glycogen, was added to 100 ml of the sample. The results were 43, less than 1 less than 1 and less for Heterotrophic, Coliform, E coli and microfungi respectively, compared with 960, 45, 15 and 5 for the reference (untreated water). **Antimicrobial**; Cleaning

ADVANTAGE - The method is improved over prior art.

Dwg.0/0

L13 ANSWER 17 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 11
AN 1999:483780 BIOSIS

DN PREV199900483780
TI Myticin, a novel cysteine-rich **antimicrobial peptide** isolated from haemocytes and plasma of the **mussel** **Mytilus** galloprovincialis.
AU Mitta, Guillaume; Hubert, Florence; Noel, Thierry; Roch, Philippe (1)
CS (1) UMR 219 DRIM, Universite de Montpellier 2, place Eugene Bataillon, F-34095, Montpellier France
SO European Journal of Biochemistry, (Oct., 1999) Vol. 265, No. 1, pp. 71-78. ISSN: 0014-2956.
DT Article
LA English
SL English
AB We report here the isolation of two isoforms of a novel cysteine-rich **peptide** from haemocytes (isoform A of 4.438 Da and B of 4.562 Da) and plasma (isoform A) of the **mussel**, **Mytilus** galloprovincialis. The two molecules display antibacterial activity against gram-positive bacteria, whereas only isoform B is active against the fungus Fusarium oxysporum and a gram-negative bacteria Escherichia coli D31. Complete **peptide** sequences were determined by a combination of Edman degradation, mass spectrometry and cDNA cloning using a haemocyte cDNA library. The mature molecules, named myticins, comprise 40 residues with four intramolecular disulfide bridges and a cysteine array in the primary structure different to that of the previously characterized cysteine-rich **antimicrobial peptides**. Sequence analysis of the cloned cDNAs revealed that myticin precursors consist of 96 amino acids with a putative signal **peptide** of 20 amino acids, the **antimicrobial peptide** sequence and a 36-residue C-terminal extension. This structure suggests that myticins are synthesized as preproproteins and then processed by various proteolytic events before storage of the active **peptide** in the haemocytes. Myticin precursors are expressed mainly in the haemocytes as revealed by Northern blot analysis.

L13 ANSWER 18 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
AN 1996:463635 BIOSIS
DN PREV199699185991
TI Innate immunity: Isolation of several cysteine-rich **antimicrobial** **peptides** from the blood of a **mollusc**, **Mytilus** edulis.
AU Charlet, Maurice; Chernysh, Serguey; Philippe, Herve; Hertu, Charles; Hoffmann, Jules A.; Bulet, Philippe (1)
CS (1) Unite Prope de Recherche 9022 reponse Immunitaire, Dev. chez les Insectes, CNRS, Inst. de Biol. Moleculaire Cellulaire, 15 rue Rene Descartes, 67084 Strasbourg Cedex France
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 36, pp. 21808-21813. ISSN: 0021-9258.
DT Article
LA English
AB We have isolated from the blood of immune-challenged and untreated mussels (**Mytilus** edulis) antibacterial and antifungal **peptides** . We have characterized two isoforms of a novel 34-residue, cysteine-rich, **peptide** with potent bactericidal activity and partially characterized a novel 6.2-kDa antifungal **peptide** containing 12 cysteines. We report the presence of two members of the insect defensin family of antibacterial **peptides** and provide a phylogenetic analysis that indicates that **mollusc**, and arthropod defensins have a common ancestry. Our data argue that circulating **antimicrobial peptides** represent an ancient host defense mechanism that predated the separation between **molluscs** and arthropods at the root of the Cambrian, about 545 million years ago.

L13 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1994:210809 CAPLUS
DN 120:210809
TI **Antimicrobial** glycoprotein from mussels.
IN De Faire, Johan
PA Phairson Medical AB, Swed.
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9404033	A1	19940303	WO 1993-SE684	19930817
	W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	EP 654968	A1	19950531	EP 1994-908144	19930817
	EP 654968	B1	19981104		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	AU 671481	B2	19960829	AU 1993-47674	19930817
	AU 9347674	A1	19940315		
	AT 172848	E	19981115	AT 1994-908144	19930817
	BR 9306913	A	19981208	BR 1993-6913	19930817
	ES 2125440	T3	19990301	ES 1994-908144	19930817
	AT 180141	E	19990615	AT 1994-908144	19930817
	JP 3000299	B2	20000117	JP 1994-506165	19930817
	JP 08500588	T2	19960123		
	US 5817618	A	19981006	US 1995-379568	19950210
	NO 9500565	A	19950215	NO 1995-565	19950215
	FI 9500694	A	19950216	FI 1995-694	19950216
	US 5763472	A	19980609	US 1996-738112	19961025
PRAI	SE 1992-2362	A	19920817		
	WO 1993-SE684	W	19930817		
	US 1995-379568	A3	19950210		

AB An microbicide, esp. useful for surfaces,, liqs. and gases, comprises a **protein** isolated from mussels, preferably used together with glycogen. Quick qual. testing of contamination in liqs., esp. drinking water, is carried out using a test tube contg. a predetd. amt. of the **antimicrobial** compn. A predetd. amt. of the liq. is added to the test tube, shaken and allowed to sediment. The quality of the liq. is detd. by an indicator extending along the tube. A glycoprotein (mol.-wt. 12,000-30,000) was sepd. from **Mytilus** edulis processing wastewaters by adsorption on hydroxyapatite and elution with 0.01-0.5 M NaCl, followed by purifn. by dialysis. The glycoproteins are resistant to proteolysis with trypsin or papain.

L13 ANSWER 20 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 13
AN 1981-87230D [47] WPIDS
TI Poly **peptide** fraction from mussels which binds sialic acids - useful as **antimicrobial**, esp. antiviral and antibacterial agent.
DC B04
PA (PHAA) PHARMACIA AB; (ROTH-I) ROTHMAN U S E
CYC 14
PI WO 8103124 A 19811112 (198147)* EN 18p
RW: AT CH DE FR GB LU NL SE
W: AU DK FI JP US
SE 8003253 A 19811130 (198151)
SE 8003256 A 19811130 (198151)
EP 50636 A 19820505 (198219) EN
R: AT CH DE FR GB LI LU NL SE
DK 8105771 A 19820524 (198224)

JP 57500784 W 19820506 (198224)
FI 8104188 A 19820831 (198238)
EP 50636 B 19840801 (198431) EN
R: AT CH DE FR GB LI LU NL SE
DE 3165190 G 19840906 (198437)
US 4550020 A 19851029 (198546)
JP 04053849 B 19920827 (199239) 9p
ADT EP 50636 A EP 1981-901117 19810429; US 4550020 A US 1981-336400 19811223;
JP 04053849 B JP 1981-501488 19810429, WO 1981-SE130 19810429
FDT JP 04053849 B Based on JP 57500784, Based on WO 8103124
PRAI SE 1980-3253 19800429; SE 1980-3256 19800429
AB WO 8103124 A UPAB: 19930915
A polypeptide fraction (I), for use as an **antimicrobial**, isolated from the body liqs. of **mussel** and capable of biospecifically binding at least one sialic acid (II), opt. in presence of calcium ions, is new. (I) is pref. isolated from **Mytilus** species, esp. **Mytilus** edulis (blue **mussel**).

(II) are N- and/or O-acyl derivs. of neuraminic acid. (I) is isolated e.g. by extracting the body fluids of mussels then sepg. (I) by affinity chromatography.

(I) can be used (1) as an immunising (including local immunisation) agent and as a vaccine against viral infections (esp. those caused by Myxo viruses, partic. influenza virus), (2) as an antibacterial esp. for topical treatment of body cavities to prevent or inhibit bacterial attacks in wounds, mucous membranes and bone surfaces and for prophylaxis and treatment of intestinal infections (e.g. those caused by giardiasis, amoebiasis and entamoeba histdytica); and (3) to prepare antisera by injecting into a host animal then removing blood when the desired amt. of antibodies has formed.

=> d his

(FILE 'HOME' ENTERED AT 16:30:37 ON 10 SEP 2003)

FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS, LIFESCI, CAPLUS' ENTERED AT 16:30:58 ON 10 SEP 2003

E ROCH PHILIPPE/AU
L1 75 S E3
E MITTA GUILLAUME/AU
L2 56 S E2-E3
E HUBERT FLORENCE/AU
L3 17 S E3
E NOEL THIERRY/AU
L4 27 S E3
L5 134 S L1-L4
L6 13 S L5 AND MYTICIN
L7 5 DUP REM L6 (8 DUPLICATES REMOVED)
L8 13 S L5 AND ANTIMICROBIAL PEPTIDE
L9 8 DUP REM L8 (5 DUPLICATES REMOVED)
L10 398 S ANTIMICROBIAL AND (MOLLUSC? OR MUSSEL)
L11 68 S L10 AND MYTILUS
L12 54 S L11 AND (PROTEIN OR PEPTID?)
L13 20 DUP REM L12 (34 DUPLICATES REMOVED)

=> s antibacterial and (mollusc? or mussel)
L14 487 ANTIBACTERIAL AND (MOLLUSC? OR MUSSEL)

=> s l14 and mytilus
L15 68 L14 AND MYTILUS

=> s l15 and (protein or peptid?)
L16 50 L15 AND (PROTEIN OR PEPTID?)

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17 17 DUP REM L16 (33 DUPLICATES REMOVED)

=> d bib ab 1-17

L17 ANSWER 1 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 2003:129472 BIOSIS
DN PREV200300129472
TI The influence of temperature and dose on **antibacterial peptide** response against lipopolysaccharide in the blue **mussel**, **Mytilus** edulis.
AU Hernroth, B. (1)
CS (1) Kristineberg Marine Research Station, The Royal Swedish Academy of Sciences, S-450 34, Fiskebackskil, Sweden Sweden
SO Fish & Shellfish Immunology, (January 2003, 2003) Vol. 14, No. 1, pp. 25-37. print.
ISSN: 1050-4648.
DT Article
LA English
AB Blue mussels (**Mytilus** edulis) were inoculated with two different doses of lipopolysaccharides (LPS) or phosphate-saline (PS) buffer under different temperature conditions (6 and 20degree C). The activity of the **antibacterial peptide** fraction, purified through reverse phase chromatography from **mussel** haemolyph, was compared at different time intervals after the inoculation. The activity was determined as the minimal **peptide** concentration that inhibited growth of the Gram-negative bacteria Escherichia coli D21, by using radial diffusion assay. The **antibacterial** activity for mussels inoculated with LPS changed over time, both at 6 and 20degree C, but those inoculated with PS-buffer did not. The response was enhanced within a time course of 3 h. The higher temperature did increase the inhibitory activity and made the **mussel** respond at an earlier stage, in comparison to that at 6degree C. At 20degree C, mussels inoculated with 10 mug of LPS responded faster than those inoculated with 0.1 mug of LPS. In addition, cytotoxic effects of LPS on **mussel** haemocytes were investigated in vitro, using a colorimetric assay. The survival index (SI%) for haemocytes decreased with 76% at 6degree C but increased with 100% at 20degree C, irrespective of the dose of LPS. This indicated that LPS did not influence the viability of the haemocytes but the high temperature increased their metabolic state. Likely, **antibacterial** response was provoked by LPS in a dose-dependent manner and favoured by higher metabolic state of the haemocytes, elicited at higher temperature. These results provide important considerations for variability in the internal defence of mussels and consequently, also the retention of viable human pathogens in mussels.

L17 ANSWER 2 OF 17 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN DUPLICATE 2
AN 2001-149782 [16] WPIDS
DNC C2001-044468
TI New antimicrobial **peptides** myticines obtainable from a bivalve **mollusc**, especially **Mytilus** galloprovincialis are useful for treatment and prevention of microbial disease.
DC B04 D16
IN HUBERT, F; MITTA, G; NOEL, T; ROCH, P
PA (CNRS) CNRS CENT NAT RECH SCI; (IFRE-N) IFREMER INST FR RECH EXPL MER; (FRRE-N) INST FR RECH EXPL MER
CYC 95
PI FR 2796072 A1 20010112 (200116)* 18p
WO 2001004294 A1 20010118 (200116) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2000062962 A 20010130 (200127)
EP 1194550 A1 20020410 (200232) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003504055 W 20030204 (200320) 23p
ADT FR 2796072 A1 FR 1999-8858 19990708; WO 2001004294 A1 WO 2000-FR1975 20000707; AU 2000062962 A AU 2000-62962 20000707; EP 1194550 A1 EP 2000-949681 20000707, WO 2000-FR1975 20000707; JP 2003504055 W WO 2000-FR1975 20000707, JP 2001-509498 20000707
FDT AU 2000062962 A Based on WO 2001004294; EP 1194550 A1 Based on WO 2001004294; JP 2003504055 W Based on WO 2001004294
PRAI FR 1999-8858 19990708
AB FR 2796072 A UPAB: 20010323
NOVELTY - New antimicrobial **peptides** (I), myticines, obtainable from a bivalve **mollusc**, have a molecular weight of about 4.5 kD, have an isoelectric point of about 8.7 and comprise 8 cysteine residues.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a nucleic acid (II) comprising a sequence encoding (I);
(2) an oligonucleotide comprising a segment of at least 15 base pairs (bp) of the nucleic acid of (1);
(3) an expression cassette comprising (II) under the transcriptional control of a promoter;
(4) a recombinant vector comprising (II);
(5) a prokaryotic or eukaryotic cell transformed with (II);
(6) production of (I) by expression of (II) in the cell of (5).
ACTIVITY - Antimicrobial; **antibacterial**; fungicidal.
Myticine a had a minimum bactericidal concentration of 2.25-4.5 against Micrococcus luteus and Bacillus megaterium and 4.5-9 against Aerococcus viridans and was inactive against other Gram-positive and -negative bacteria tested and against Fusarium oxysporum and the oyster parasite Perkinsus marinus.
MECHANISM OF ACTION - None given.
USE - (I) have **antibacterial** and fungicidal activity and can be used to prepare anti-infective medicaments and to prevent and treat microbial diseases in various sectors, e.g. health, agriculture, aquaculture and animal husbandry.
Dwg.0/0

L17 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:50800 CAPLUS
DN 134:111262
TI **Mytilus** myticins and cDNAs, their production with recombinant cells, and their use as antimicrobial agents
IN Roch, Philippe; Mitta, Guillaume; Hubert, Florence; Noel, Thierry
PA Centre National de la Recherche Scientifique (CNRS), Fr.; Institut Francais de Recherche pour l'Exploitationde La Mer (IFREMER)
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001004294	A1	20010118	WO 2000-FR1975	20000707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2796072 A1 20010112 FR 1999-8858 19990708
EP 1194550 A1 20020410 EP 2000-949681 20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 2003504055 T2 20030204 JP 2001-509498 20000707
PRAI FR 1999-8858 A 19990708
WO 2000-FR1975 W 20000707

AB The invention concerns an antimicrobial **peptide**, called myticin, characterized in that it can be obtained from a bivalve **mollusc** shellfish, and its mol. mass is about 4.5 kDa; its pI is about 8.7; it comprises 8 cysteines. The invention also concerns its prepn. and its uses. The invention further concerns a nucleic acid coding for said **peptide**. Thus, myticins a and b were purified from **Mytilus** galloprovincialis and their **antibacterial**, antifungal, and antiprotozoal activities examd. Addnl., the cDNAs encoding the prepromyticins were cloned and sequenced.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:509580 CAPLUS
TI Solution structure and activity of the synthetic Mediterranean **mussel** defensin (MGD-1)
AU Aumelas, Andre; Yang, Yin-Shan; Mitta, Guillaume; Chavanieu, Alain; Sanchez, Jean-Frederic; Calas, Bernard; Roch, Philippe
CS Centre de Biochimie Structurale, Faculte de Pharmacie, UMR 5048, U414 INSERM, Universite Montpellier 1, Montpellier, 34060, Fr.
SO Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 447-448. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Publisher: Editions EDK, Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DT Conference
LA English
AB The anti-bacterial activity and soln. structure of synthetic Mediterranean **mussel** defensin, **Mytilus** Galloprovincialis defensin, (MGD-1) were investigated. 1H-NMR established the soln. structure of solid-phase synthesized MGD-1 **peptide**. The synthetic MGD-1 soln. structure consists of the canonical CS.alpha..beta., made up of an .alpha.-helical part (residues 7-16) and of a slightly twisted .beta.-sheet made up of two strands, spanning residues 20-25 and 33-37. These various elements of secondary structure are tightly cross-linked by four disulfide bonds (Cys4-Cys25, Cys10-Cys33, Cys14-Cys35 and Cys21-Cys38). Three of them are located in the hydrophobic core of the mol., whereas the fourth (Cys21-Cys38), which is specific for the MGD-1 structure, is solvent exposed. The Cys4-Pro5 amide bond was found to adopt the unusual cis conformation. MGD-1 and Defensin A structures share some common properties, namely, in terms of their 3D structure and the distribution of hydrophobic and hydrophilic side chains which could explain their similar activity against Gram-pos. bacteria.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 2002:117723 BIOSIS
DN PREV200200117723

TI **Antibacterial** activities of oyster (Crassostrea virginica) and **mussel** (**Mytilus** edulis and Geukensia demissa) plasma.
AU Anderson, Robert S. (1); Beaven, Amy E.
CS (1) Chesapeake Biological Laboratory, University of Maryland Center for Environmental Science, Solomons, MD, 20688: anderson@cbl.umces.edu USA
SO Aquatic Living Resources, (November December, 2001) Vol. 14, No. 6, pp. 343-349. print.
ISSN: 0990-7440.
DT Article
LA English
AB Anti-Bacillus megaterium activity was measured in unfractionated plasma withdrawn from three common US East Coast bivalve **molluscs**: an oyster Crassostrea virginica and the mussels Geukensia demissa and **Mytilus** edulis. The activities of the plasma samples from these bivalves were also measured against a C. virginica pathogen Perkinsus marinus. Strong anti-B. megaterium activity was measured in plasma from C. virginica and M. edulis, but was not detected in G. demissa. Bactericidal activity was found in hemocyte extracts from all bivalves in this study, suggesting a cellular origin of cytotoxic humoral factors. **Peptides** (< 10 kDa) were separated from the plasma samples by ultrafiltration; weak **antibacterial peptide** activity was quantified in C. virginica **peptides**, but not in **peptides** from the mussels. In the case of P. marinus, plasma from M. edulis or G. demissa was strongly cidal as compared to plasma from C. virginica. This difference in activity probably reflects the low pathogenicity of this oyster parasite for the **mussel** species tested. In summary, the bactericidal activity of plasma proteins from these bivalves showed considerable interspecies variation and did not necessarily correlate directly with antiprotistan activity. When present, **antibacterial** and antiprotistan activities seemed to be associated with plasma proteins rather than < 10-kDa plasma **peptides**, with the possible exception of C. virginica anti-B. megaterium activity and the occasionally expressed anti-P. marinus activity of M. edulis **peptides**. The precise identity of the plasma **protein**(s) responsible for the antimicrobial activities measured have yet to be determined, but it is likely that agents other than, or in addition to, lysozyme play significant roles in the process.

L17 ANSWER 6 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 4
AN 2002:175305 BIOSIS
DN PREV200200175305
TI Solution structure and activity of the synthetic four-disulfide bond Mediterranean **mussel** defensin (MGD-1.
AU Yang, Yin-Shan; Mitta, Guillaume; Chavanieu, Alain; Calas, Bernard; Sanchez, Jean Frederic; Roch, Philippe; Aumelas, Andre (1)
CS (1) Centre de Biochimie Structurale, Faculte de Pharmacie, CNRS UMR 5048, INSERM U414, 15 Avenue Charles Flahault, F-34060, Montpellier Cedex 2: aumelas@cbs.univ-montpl.fr France
SO Biochemistry, (November 28, 2000) Vol. 39, No. 47, pp. 14436-14447. http://pubs.acs.org/journals/bichaw/. print.
ISSN: 0006-2960.
DT Article
LA English
AB MGD-1 is a 39-residue defensin-like **peptide** isolated from the edible Mediterranean **mussel**, **Mytilus** galloprovincialis. This **peptide** is characterized by the presence of four disulfide bonds. We report here its solid-phase synthesis and an easy way to improve the yield of the four native disulfide bonds. Synthetic and native MGD-1 display similar **antibacterial** activity, suggesting that the hydroxylation of Trp28 observed in native MGD-1 is not involved in the antimicrobial effect. The three-dimensional solution structure of MGD-1 has been established using 1H NMR and mainly

consists of a helical part (Asn7-Ser16) and two antiparallel beta-strands (Arg20-Cys25 and Cys33-Arg37), together giving rise to the common cystine-stabilized alpha-beta motif frequently observed in scorpion toxins. In MGD-1, the cystine-stabilized alpha-beta motif is stabilized by four disulfide bonds (Cys4-Cys25, Cys10-Cys33, Cys14-Cys35, and Cys21-Cys38), instead of by the three disulfide bonds commonly found in arthropod defensins. Except for the Cys21-Cys38 disulfide bond which is solvent-exposed, the three others belong to the particularly hydrophobic core of the highly constrained structure. Moreover, the C4-P5 amide bond in the cis conformation characterizes the MGD-1 structure. MGD-1 and insect defensin A possess similar bactericidal anti-Gram-positive activity, suggesting that the fourth disulfide bond of MGD-1 is not essential for the biological activity. In agreement with the general features of **antibacterial peptides**, the MGD-1 and defensin A structures display a typical distribution of positively charged and hydrophobic side chains. The positively charged residues of MGD-1 are located in three clusters. For these two defensin **peptides** isolated from insects and mollusks, it appears that the rather well conserved location of certain positively charged residues and of the large hydrophobic cluster are enough to generate the bactericidal potency and the Gram-positive specificity.

L17 ANSWER 7 OF 17 LIFESCI COPYRIGHT 2003 CSA on STN
AN 2000:104714 LIFESCI
TI Involvement of Mytilins in **Mussel** Antimicrobial Defense
AU Mitta, G.; Vandenbulcke, F.; Hubert, F.; Salzet, M.; Roch, P.
CS Defense et Resistance chez les Invertebres Marins, IFREMER-CNRS, Universite de Montpellier 2, cc 80, 34095 Montpellier, France; E-mail: proch@ifremer.fr.
SO Journal of Biological Chemistry [J. Biol. Chem.], (20000428) vol. 275, no. 17, pp. 12954-12962.
ISSN: 0021-9258.
DT Journal
FS A
LA English
SL English
AB Four cationic **peptides** were purified from **mussel** (**Mytilus** galloprovincialis) hemocytes. A combination of Edman degradation and mass spectrometry of plasma revealed (i) a previously characterized molecule, mytilin B (Charlet, M., Chernysh, S., Philippe, H., Hetrut, C., Hoffmann, J., and Bulet, P. (1996) J. Biol. Chem. 271, 21808-21813) and (ii) three new isoforms, mytilin C, D, and G1. The four molecules exhibited complementary antimicrobial properties. The cDNA sequence coding for the mytilin B precursor was obtained from a hemocyte cDNA library. This precursor contains a putative signal **peptide** of 22 residues, a processing **peptide** sequence of 34 amino acids, and a C-terminal extension of 48 residues rich in acidic residues. Distribution of mytilin B mRNA and of the corresponding **peptide** in various **mussel** tissues revealed that mytilins are synthesized and stored in a specific hemocyte subtype. Furthermore, in an experimental model of infection, we showed (i) a recruitment of hemocytes containing mytilins toward the injection site within hours following bacterial challenge, (ii) that mytilins probably play a prominent role in killing intracellular bacteria after phagocytosis, and (ii) later an increase of mytilin-like material occurred in the plasma suggesting a secondary systemic role.

L17 ANSWER 8 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
AN 2000:260739 BIOSIS
DN PREV200000260739
TI Proenkephalin A-derived **peptides** in invertebrate innate immune processes.

AU Tasiemski, Aurelie; Verger-Bocquet, Martine; Cadet, Mario; Goumon, Yannick; Metz-Boutigue, Marie-Helene; Aunis, Dominique; Stefano, George B.; Salzet, Michel (1)

CS (1) Laboratoire d'Endocrinologie des Annelides, UPRES-A CNRS 8017, SN3, Universite des Sciences et Technologies de Lille, F-59655, Villeneuve d'Ascq Cedex France

SO Molecular Brain Research, (March 29, 2000) Vol. 76, No. 2, pp. 237-252. print..
ISSN: 0169-328X.

DT Article

LA English

SL English

AB Lipopolysaccharides (LPS) injection into the coelomic fluid of the leech Theromyzon tessulatum stimulates release of proenkephalin A (PEA)-derived **peptides** as determined by immunoprecipitation and Western blot analyses. This release occurs in the first 15 min after LPS exposure and yields a 5.3-kDa **peptide** fragment corresponding to the C-terminal part of the precursor. This fragment is then cleaved to free an **antibacterial peptide** related to mammals arginine phenylalanine extended enkelytin: the **peptide** B. These PEA processing **peptides** were characterized using a combination of techniques including reversed-phase HPLC, microsequencing and mass spectrometry. The isolated invertebrate **peptide** B presents a high sequence homology with the bovine's and the same activity against Gram + bacteria. Titrations revealed the simultaneous appearance of Methionine-enkephalin (ME) and **peptide** B in invertebrates after stimulation by LPS (in a dose-dependent manner), surgical trauma or electrical stimulations to neural tissues of the **mussel**. Furthermore, **peptide** B processing in vitro yields Methionine-enkephalin arginine phenylalanine (MERF), which exhibits via the delta receptors, immunocyte excitatory properties, i.e., movement and conformational changes, but no **antibacterial** activity. We surmise that this unified response to the various stimuli is a survival strategy for organism by providing immediate **antibacterial** activity and immunocyte stimulation, thereby reducing any immune latency period needed for an adequate immune response.

L17 ANSWER 9 OF 17 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1999-312395 [26] WPIDS

DNC C1999-092172

TI Antimicrobial composition containing active **protein** isolated from mussels and carbohydrates, used for cleaning contaminated tissues or treating wounds.

DC B04 B07 D22

IN DE FAIRE, J

PA (MICR-N) MICRO ACTIVE PROTEIN IN SWEDEN AB

CYC 82

PI WO 9909835 A1 19990304 (199926)* EN 14p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9888950 A 19990316 (199930)

ADT WO 9909835 A1 WO 1998-SE1510 19980824; AU 9888950 A AU 1998-88950 19980824

FDT AU 9888950 A Based on WO 9909835

PRAI SE 1997-3085 19970827

AB WO 9909835 A UPAB: 19990707
NOVELTY - The use of a composition containing at least one antimicrobially active **protein** (I), isolated from mussels and carbohydrates, is claimed in a product having antimicrobial activity and coagulant effect, for:

(a) treating and cleaning microbially contaminated tissues, body surfaces or cavities, and/or

(b) treating bleeding wounds, lesions and damaged tissues.

ACTIVITY - **Antibacterial**; coagulant. Test samples were prepared by dissolving lyophilized powder comprising active **protein** isolated from **Mytilus** edulis in 0.9% saline ((A) 0.005, (B) 0.05 or (C) 0.5 mu g/ml). Test samples or saline (20 mu l) were added to fresh blood (200 mu l) on glass slides. The slides were held vertically every 15 seconds, and time to clotting determined. Results for clotting times (seconds) were: (A) 120, (B) 90 and (C) 90, compared with 195 for the saline control and 165 for blood alone.

MECHANISM OF ACTION - None given.

USE - The product is for external use, e.g. as an adhesive dressing, a band aid, bandage or dressing; or for internal use, e.g. as a suture thread, catheter or an implant (optionally biodegradable). Such products improve blood coagulation and prevent tissue adhesion.

ADVANTAGE - Use of the composition results in decreased bleeding time of bleeding wounds and improved tissue healing.

L17 ANSWER 10 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6
AN 2000:103097 BIOSIS
DN PREV200000103097
TI **Mussel** defensins are synthesised and processed in granulocytes then released into the plasma after bacterial challenge.
AU Mitta, Guillaume; Vandenbulcke, Franck; Hubert, Florence; Roch, Philippe (1)
CS (1) Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER-CNRS-Universite de Montpellier 2, 34095, Montpellier France
SO Journal of Cell Science, (Dec., 1999) Vol. 112, No. 23, pp. 4233-4242. ISSN: 0021-9533.
DT Article
LA English
SL English
AB MGD1 (**Mytilus** galloprovincialis defensin 1), a new member of the arthropod defensin family, is a 4 kDa **antibacterial peptide** previously isolated from the plasma of Mediterranean mussels. We report here the presence of MGD1 in the organelle-rich fraction of hemocytes and the cDNA sequence corresponding to MGD1 and one new isoform mRNA: MGD2. Sequence analysis indicated that MGDs are synthesised as precursors consisting of a putative signal **peptide** of 21 residues, the active **peptide** of 39 amino acids and a 21 residue carboxyl-terminal extension, rich in acidic amino acids. Localisation of the transcripts by northern blot revealed that the precursors are abundantly expressed in hemocytes. Immunocytochemistry at both the optical and ultrastructural levels showed that defensins (i) are predominantly located in vesicles of a granulocyte subclass of hemocytes containing small granules, (ii) are also found in large clear granules of another granulocyte subclass, and (iii) that MGD immune reactivity existed in granular structures of enterocytes. Finally, we revealed that bacterial challenge triggered a plasmatic increase of MGD1 concentration and gave evidence of the simultaneous release of the **peptides** from the hemocytes.

L17 ANSWER 11 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7
AN 1999:483780 BIOSIS
DN PREV199900483780
TI Myticin, a novel cysteine-rich antimicrobial **peptide** isolated from haemocytes and plasma of the **mussel Mytilus** galloprovincialis.
AU Mitta, Guillaume; Hubert, Florence; Noel, Thierry; Roch, Philippe (1)
CS (1) UMR 219 DRIM, Universite de Montpellier 2, place Eugene Bataillon,

F-34095, Montpellier France
SO European Journal of Biochemistry, (Oct., 1999) Vol. 265, No. 1, pp. 71-78. ISSN: 0014-2956.
DT Article
LA English
SL English
AB We report here the isolation of two isoforms of a novel cysteine-rich **peptide** from haemocytes (isoform A of 4.438 Da and B of 4.562 Da) and plasma (isoform A) of the **mussel**, **Mytilus** galloprovincialis. The two molecules display **antibacterial** activity against gram-positive bacteria, whereas only isoform B is active against the fungus Fusarium oxysporum and a gram-negative bacteria Escherichia coli D31. Complete **peptide** sequences were determined by a combination of Edman degradation, mass spectrometry and cDNA cloning using a haemocyte cDNA library. The mature molecules, named myticins, comprise 40 residues with four intramolecular disulfide bridges and a cysteine array in the primary structure different to that of the previously characterized cysteine-rich antimicrobial **peptides**. Sequence analysis of the cloned cDNAs revealed that myticin precursors consist of 96 amino acids with a putative signal **peptide** of 20 amino acids, the antimicrobial **peptide** sequence and a 36-residue C-terminal extension. This structure suggests that myticins are synthesized as preproproteins and then processed by various proteolytic events before storage of the active **peptide** in the haemocytes. Myticin precursors are expressed mainly in the haemocytes as revealed by Northern blot analysis.

L17 ANSWER 12 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8
AN 1997:504885 BIOSIS
DN PREV199799804088
TI Invertebrate proenkephalin: delta opioid binding sites in leech ganglia and immunocytes.
AU Salzet, Michel; Stefano, George B. (1)
CS (1) Centre de Biologie Cellulaire, Laboratoire de Phylogenie Moleculaire des Annelides EA DRED 1027, Groupe de Neuroendocrinologie des Hirudinees, Universite des Sciences et Technologies de Lille, 59655 Villeneuve d'Ascq Cedex France
SO Brain Research, (1997) Vol. 768, No. 1-2, pp. 224-232. ISSN: 0006-8993.
DT Article
LA English
AB The leech Theromyzon tessulatum and the marine **mussel** **Mytilus** edulis immunocytes contain a mammalian-like proenkephalin molecule. The opioid precursor was purified by gel permeation chromatography, anti-Met- and Leu-enkephalin-affinity column separation and then by reversed-phase HPLC. The amino acid sequence analysis, determined by Edman degradation, enzymatic treatments and matrix assisted laser desorption time of flight. The structure of the leech proenkephalin material demonstrates considerable amino acid sequence similarity with amphibian proenkephalin (e.g. 25.4% with Xenopus laevis) but it is smaller, 15 kDa vs. 30 kDa. In contrast, **Mytilus** proenkephalin is not only larger (26 kDa) but it exhibits a higher sequence identity with guinea pig proenkephalin (50%). Both of the invertebrate materials possess Met-enkephalin and Leu-enkephalin in a ratio of 3:1 for **Mytilus** and 1:2 in the leech. They also contain Met-enkephalin-Arg-Gly-Leu and Met-enkephalin-Arg-Phe sequences that are flanked by dibasic amino acid residues, demonstrating cleavage sites. Furthermore, using sequence comparison with bovine proenkephalin A (209-237), enkelytin (FAEPLPSEEEGESYSKEVPEMEKRYGGFM), an **antibacterial peptide** is found in the proenkephalin of both animals and it exhibits a 98% sequence identity with mammalian material. Finally, opioid binding experiments demonstrate the presence in

leech ganglia and immunocytes of delta-1 and delta-2 opioid receptor subtypes as also found human and **Mytilus** immune cells. This report constitutes the first complete biochemical characterization of mammalian proenkephalin in invertebrates, demonstrating its origin in simpler animals.

L17 ANSWER 13 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9
AN 1997:367372 BIOSIS
DN PREV199799659305
TI Structure and differential target sensitivity of the stimulable cytotoxic complex from hemolymph of the Mediterranean **mussel** **Mytilus** galloprovincialis.
AU Hubert, Florence; Cooper, Edwin L.; Roch, Philippe (1)
CS (1) Univ. Montpellier 2, UMR DRIM cc 80, Place Eugene Bataillon, 34095 Montpellier Cedex France
SO Biochimica et Biophysica Acta, (1997) Vol. 1361, No. 1, pp. 29-41. ISSN: 0006-3002.
DT Article
LA English
AB A cytotoxic **protein** complex of 320 kDA was isolated from dialyzed plasma of the edible **mussel**, **Mytilus** galloprovincialis. Constituted by the assembly of several different proteins, the complex exhibits selective killing against eukaryotic cells, including erythrocytes, mouse tumor cells and protozoan parasites. High variability, which was not correlated with **protein** concentration, suggested that the immune response of naive mussels was in various stages of activation. Stimulation assays by different treatments in vivo resulted in significant increases in the activity of the plasma suggesting that cytotoxic complexes are involved in immune defense. Lytic activity appears to involve binding of cytotoxic complexes onto target cell membranes and the formation of transmembrane pores. This research provides more evidence that the innate immune system of invertebrates involves large cytotoxic proteins with a broad range of recognitive specificities in addition to small **antibacterial**, antifungal **peptides**.

L17 ANSWER 14 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 10
AN 1996:463635 BIOSIS
DN PREV199699185991
TI Innate immunity: Isolation of several cysteine-rich antimicrobial **peptides** from the blood of a **mollusc**, **Mytilus** edulis.
AU Charlet, Maurice; Chernysh, Serguey; Philippe, Herve; Hertu, Charles; Hoffmann, Jules A.; Bulet, Philippe (1)
CS (1) Unite Prope de Recherche 9022 reponse Immunitaire, Dev. chez les Insectes, CNRS, Inst. de Biol. Moleculaire Cellulaire, 15 rue Rene Descartes, 67084 Strasbourg Cedex France
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 36, pp. 21808-21813. ISSN: 0021-9258.
DT Article
LA English
AB We have isolated from the blood of immune-challenged and untreated mussels (**Mytilus** edulis) **antibacterial** and antifungal **peptides**. We have characterized two isoforms of a novel 34-residue, cysteine-rich, **peptide** with potent bactericidal activity and partially characterized a novel 6.2-kDa antifungal **peptide** containing 12 cysteines. We report the presence of two members of the insect defensin family of **antibacterial** **peptides** and provide a phylogenetic analysis that indicates that **mollusc**, and arthropod defensins have a common ancestry. Our data argue that circulating antimicrobial **peptides** represent an

ancient host defense mechanism that predated the separation between **molluscs** and arthropods at the root of the Cambrian, about 545 million years ago.

L17 ANSWER 15 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11
AN 1996:422693 BIOSIS
DN PREV199699153749
TI A member of the arthropod defensin family from edible Mediterranean mussels (**Mytilus** galloprovincialis.
AU Hubert, Florence; Noel, Thierry; Roch, Philippe (1)
CS (1) Univ. Montpellier 2, UMR DRIM, cc 80, 2 place Eugene Bataillon, F-34095 Montpellier cedex 5 France
SO European Journal of Biochemistry, (1996) Vol. 240, No. 1, pp. 302-306. ISSN: 0014-2956.
DT Article
LA English
AB Plasma from the **mussel Mytilus** galloprovincialis previously immunized by injecting them with bacteria contains several bactericidal proteins. One **protein**, MGD-1, was purified by reverse-phase HPLC of supernatant from acidified cell-free hemolymph. Its biological activity is directed against both gram-positive and gram-negative bacteria but it is not cytotoxic towards human erythrocytes nor protozoa. As determined by mass spectrometry, the molecular mass of MGD-1 is 4418 Da. Primary-structure analysis revealed 38 amino acids including 8 cysteines and a modified amino acid residue in position 28. Computer searches unambiguously recognized the signature of an arthropod defensin, but the presence of two extra cysteines and of one modified amino acid suggest that it is a previously unknown member of that family.

L17 ANSWER 16 OF 17 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
AN 1996:413731 BIOSIS
DN PREV199699136087
TI Cytotoxic and **antibacterial** properties of **Mytilus** galloprovincialis, Ostrea edulis and Crassostrea gigas (bivalve **molluscs**) hemolymph.
AU Hubert, Florence; Van Der Knaap, Wil; Noel, Thierry; Roch, Philippe
CS IFREMER-CNRS-Univ. Montpellier, 2 Defense et Resistance chez les Invertebres marins, 2 place Eugene Bataillon, 34095 Montpellier Cedex 5 France
SO Aquatic Living Resources, (1996) Vol. 9, No. 2, pp. 115-124. ISSN: 0990-7440.
DT Article
LA English
SL English; French
AB **Mussel** (**Mytilus** galloprovincialis) plasma contains cytotoxic activity against both vertebrate (erythrocytes and mouse tumour) and protozoan cells. Procaryotes (Escherichia coli and Vibrio alginolyticus) were not sensitive to the cytotoxicity. The activity was still present in dialyzed samples but was inhibited by heating at 45 degree C. Large individual variability which was not correlated with **protein** concentration and an increasing number of reactive specimens following injection, suggested that naive mussels were in various stages of immune response. Purification by anion exchange chromatography followed by gel filtration revealed a 320 kDa cytotoxic polymeric **protein** that acts through a polymerization process after binding onto target cell membranes as revealed by ultrastructural observation. European and Pacific oysters (Ostrea edulis and Crassostrea gigas) expressed **antibacterial** activity against both Gram negative and Gram positive bacteria which was most probably due to small proteins. When tested against the marine pathogenic Vibrio alginolyticus, hemocyte lysates of both species were more active than cell-free plasma.

Antibacterial activity showed significant individual variability that was dramatically reduced by stimulation through mechanical stress or injection. The number of spontaneously active Pacific oysters increased from 50 to 100% following a single injection of bacteria. These results strongly support the view that bivalve **molluscs** possess sensitive immuno-defense mechanisms that will greatly aid the development of aquaculture systems by employing refined techniques of transgenesis.

L17 ANSWER 17 OF 17 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1981-87230D [47] WPIDS
TI Poly **peptide** fraction from mussels which binds sialic acids - useful as antimicrobial, esp. antiviral and **antibacterial** agent.
DC B04
PA (PHAA) PHARMACIA AB; (ROTH-I) ROTHMAN U S E
CYC 14
PI WO 8103124 A 19811112 (198147)* EN 18p
RW: AT CH DE FR GB LU NL SE
W: AU DK FI JP US
SE 8003253 A 19811130 (198151)
SE 8003256 A 19811130 (198151)
EP 50636 A 19820505 (198219) EN
R: AT CH DE FR GB LI LU NL SE
DK 8105771 A 19820524 (198224)
JP 57500784 W 19820506 (198224)
FI 8104188 A 19820831 (198238)
EP 50636 B 19840801 (198431) EN
R: AT CH DE FR GB LI LU NL SE
DE 3165190 G 19840906 (198437)
US 4550020 A 19851029 (198546)
JP 04053849 B 19920827 (199239) 9p
ADT EP 50636 A EP 1981-901117 19810429; US 4550020 A US 1981-336400 19811223; JP 04053849 B JP 1981-501488 19810429, WO 1981-SE130 19810429
FDT JP 04053849 B Based on JP 57500784, Based on WO 8103124
PRAI SE 1980-3253 19800429; SE 1980-3256 19800429
AB WO 8103124 A UPAB: 19930915
A polypeptide fraction (I), for use as an antimicrobial, isolated from the body liqs. of **mussel** and capable of biospecifically binding at least one sialic acid (II), opt. in presence of calcium ions, is new. (I) is pref. isolated from **Mytilus** species, esp. **Mytilus** edulis (blue **mussel**).

(II) are N- and/or O-acyl derivs. of neuraminic acid. (I) is isolated e.g. by extracting the body fluids of mussels then sepg. (I) by affinity chromatography.

(I) can be used (1) as an immunising (including local immunisation) agent and as a vaccine against viral infections (esp. those caused by Myxo viruses, partic. influenza virus), (2) as an **antibacterial** esp. for topical treatment of body cavities to prevent or inhibit bacterial attacks in wounds, mucous membranes and bone surfaces and for prophylaxis and treatment of intestinal infections (e.g. those caused by giardiasis, amoebiasis and entamoeba histdytica); and (3) to prepare antisera by injecting into a host animal then removing blood when the desired amt. of antibodies has formed.

=> s antifungal and (mollusc? or mussel)
L18 371 ANTIFUNGAL AND (MOLLUSC? OR MUSSEL)

=> s l18 and mytilus
L19 11 L18 AND MYTILUS

=> s l19 and (protein or peptid?)
L20 10 L19 AND (PROTEIN OR PEPTID?)

=> dup rem l20
PROCESSING COMPLETED FOR L20
L21 4 DUP REM L20 (6 DUPLICATES REMOVED)

=> d bib ab 1-4

L21 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:50800 CAPLUS
DN 134:111262
TI **Mytilus** myticins and cDNAs, their production with recombinant cells, and their use as antimicrobial agents
IN Roch, Philippe; Mitta, Guillaume; Hubert, Florence; Noel, Thierry
PA Centre National de la Recherche Scientifique (CNRS), Fr.; Institut Francais de Recherche pour l'Exploitationde La Mer (IFREMER)
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001004294	A1	20010118	WO 2000-FR1975	20000707
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2796072	A1	20010112	FR 1999-8858	19990708
EP 1194550	A1	20020410	EP 2000-949681	20000707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003504055	T2	20030204	JP 2001-509498	20000707
PRAI FR 1999-8858	A	19990708		
WO 2000-FR1975	W	20000707		

AB The invention concerns an antimicrobial **peptide**, called myticin, characterized in that it can be obtained from a bivalve **mollusc** shellfish, and its mol. mass is about 4.5 kDa; its pI is about 8.7; it comprises 8 cysteines. The invention also concerns its prepn. and its uses. The invention further concerns a nucleic acid coding for said **peptide**. Thus, myticins a and b were purified from **Mytilus** galloprovincialis and their antibacterial, **antifungal**, and antiprotozoal activities examd. Addnl., the cDNAs encoding the prepromyticins were cloned and sequenced.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 4 MEDLINE on STN
AN 1999421718 MEDLINE
DN 99421718 PubMed ID: 10491159
TI Myticin, a novel cysteine-rich antimicrobial **peptide** isolated from haemocytes and plasma of the **mussel Mytilus** galloprovincialis.
AU Mitta G; Hubert F; Noel T; Roch P
CS Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER-CNRS-UM2, Montpellier, France.
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Oct 1) 265 (1) 71-8.
Journal code: 0107600. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199911
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991122
AB We report here the isolation of two isoforms of a novel cysteine-rich **peptide** from haemocytes (isoform A of 4.438 Da and B of 4.562 Da) and plasma (isoform A) of the **mussel**, **Mytilus** galloprovincialis. The two molecules display antibacterial activity against gram-positive bacteria, whereas only isoform B is active against the fungus Fusarium oxysporum and a gram-negative bacteria Escherichia coli D31. Complete **peptide** sequences were determined by a combination of Edman degradation, mass spectrometry and cDNA cloning using a haemocyte cDNA library. The mature molecules, named myticins, comprise 40 residues with four intramolecular disulfide bridges and a cysteine array in the primary structure different to that of the previously characterized cysteine-rich antimicrobial **peptides**. Sequence analysis of the cloned cDNAs revealed that myticin precursors consist of 96 amino acids with a putative signal **peptide** of 20 amino acids, the antimicrobial **peptide** sequence and a 36-residue C-terminal extension. This structure suggests that myticins are synthesized as preproproteins and then processed by various proteolytic events before storage of the active **peptide** in the haemocytes. Myticin precursors are expressed mainly in the haemocytes as revealed by Northern blot analysis.

L21 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
AN 1997:367372 BIOSIS
DN PREV199799659305
TI Structure and differential target sensitivity of the stimulable cytotoxic complex from hemolymph of the Mediterranean **mussel** **Mytilus** galloprovincialis.
AU Hubert, Florence; Cooper, Edwin L.; Roch, Philippe (1)
CS (1) Univ. Montpellier 2, UMR DRIM cc 80, Place Eugene Bataillon, 34095 Montpellier Cedex France
SO Biochimica et Biophysica Acta, (1997) Vol. 1361, No. 1, pp. 29-41. ISSN: 0006-3002.
DT Article
LA English
AB A cytotoxic **protein** complex of 320 kDA was isolated from dialyzed plasma of the edible **mussel**, **Mytilus** galloprovincialis. Constituted by the assembly of several different proteins, the complex exhibits selective killing against eukaryotic cells, including erythrocytes, mouse tumor cells and protozoan parasites. High variability, which was not correlated with **protein** concentration, suggested that the immune response of naive mussels was in various stages of activation. Stimulation assays by different treatments in vivo resulted in significant increases in the activity of the plasma suggesting that cytotoxic complexes are involved in immune defense. Lytic activity appears to involve binding of cytotoxic complexes onto target cell membranes and the formation of transmembrane pores. This research provides more evidence that the innate immune system of invertebrates involves large cytotoxic proteins with a broad range of recognitive specificities in addition to small antibacterial, **antifungal** **peptides**.

L21 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 1996:463635 BIOSIS
DN PREV199699185991
TI Innate immunity: Isolation of several cysteine-rich antimicrobial

peptides from the blood of a **mollusc**, **Mytilus** edulis.

AU Charlet, Maurice; Chernysh, Serguey; Philippe, Herve; Hertu, Charles; Hoffmann, Jules A.; Bulet, Philippe (1)

CS (1) Unite Prope de Recherche 9022 reponse Immunitaire, Dev. chez les Insectes, CNRS, Inst. de Biol. Moleculaire Cellulaire, 15 rue Rene Descartes, 67084 Strasbourg Cedex France

SO Journal of Biological Chemistry, (1996) Vol. 271, No. 36, pp. 21808-21813. ISSN: 0021-9258.

DT Article

LA English

AB We have isolated from the blood of immune-challenged and untreated mussels (**Mytilus** edulis) antibacterial and **antifungal** **peptides**. We have characterized two isoforms of a novel 34-residue, cysteine-rich, **peptide** with potent bactericidal activity and partially characterized a novel 6.2-kDa **antifungal** **peptide** containing 12 cysteines. We report the presence of two members of the insect defensin family of antibacterial **peptides** and provide a phylogenetic analysis that indicates that **mollusc**, and arthropod defensins have a common ancestry. Our data argue that circulating antimicrobial **peptides** represent an ancient host defense mechanism that predated the separation between **molluscs** and arthropods at the root of the Cambrian, about 545 million years ago.

CS (1) Centre de Biochimie Structurale, Faculte de Pharmacie, CNRS UMR 5048, INSERM U414, 15 Avenue Charles Flahault, F-34060, Montpellier Cedex 2: aumelas@cbs.univ-montp1.fr France
SO Biochemistry, (November 28, 2000) Vol. 39, No. 47, pp. 14436-14447. http://pubs.acs.org/journals/bichaw/. print.
ISSN: 0006-2960.
DT Article
LA English
AB MGD-1 is a 39-residue defensin-like **peptide** isolated from the edible Mediterranean **mussel**, **Mytilus** galloprovincialis. This **peptide** is characterized by the presence of four disulfide bonds. We report here its solid-phase synthesis and an easy way to improve the yield of the four native disulfide bonds. Synthetic and native MGD-1 display similar antibacterial activity, suggesting that the hydroxylation of Trp28 observed in native MGD-1 is not involved in the **antimicrobial** effect. The three-dimensional solution structure of MGD-1 has been established using 1H NMR and mainly consists of a helical part (Asn7-Ser16) and two antiparallel beta-strands (Arg20-Cys25 and Cys33-Arg37), together giving rise to the common cystine-stabilized alpha-beta motif frequently observed in scorpion toxins. In MGD-1, the cystine-stabilized alpha-beta motif is stabilized by four disulfide bonds (Cys4-Cys25, Cys10-Cys33, Cys14-Cys35, and Cys21-Cys38), instead of by the three disulfide bonds commonly found in arthropod defensins. Except for the Cys21-Cys38 disulfide bond which is solvent-exposed, the three others belong to the particularly hydrophobic core of the highly constrained structure. Moreover, the C4-P5 amide bond in the cis conformation characterizes the MGD-1 structure. MGD-1 and insect defensin A possess similar bactericidal anti-Gram-positive activity, suggesting that the fourth disulfide bond of MGD-1 is not essential for the biological activity. In agreement with the general features of antibacterial **peptides**, the MGD-1 and defensin A structures display a typical distribution of positively charged and hydrophobic side chains. The positively charged residues of MGD-1 are located in three clusters. For these two defensin **peptides** isolated from insects and mollusks, it appears that the rather well conserved location of certain positively charged residues and of the large hydrophobic cluster are enough to generate the bactericidal potency and the Gram-positive specificity.

L13 ANSWER 9 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN DUPLICATE 5
AN 2000:352891 BIOSIS
DN PREV200000352891
TI Involvement of mytilins in **mussel antimicrobial** defense.
AU Mitta, Guillaume; Vandenbulcke, Franck; Hubert, Florence; Salzet, Michel; Roch, Philippe (1)
CS (1) DRIM-UMR 5098, Universite de Montpellier 2, Place Eugene Bataillon, 34095, Montpellier France
SO Journal of Biological Chemistry, (April 28, 2000) Vol. 275, No. 17, pp. 12954-12962. print.
ISSN: 0021-9258.
DT Article
LA English
SL English
AB Four cationic **peptides** were purified from **mussel** (**Mytilus** galloprovincialis) hemocytes. A combination of Edman degradation and mass spectrometry of plasma revealed (i) a previously characterized molecule, mytilin B (Charlet, M., Chernysh, S., Philippe, H., Hetrut, C., Hoffmann, J., and Bulet, P. (1996) J. Biol. Chem. 271, 21808-21813) and (ii) three new isoforms, mytilin C, D, and G1. The four molecules exhibited complementary **antimicrobial** properties. The cDNA sequence coding for the mytilin B precursor was obtained from a

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:603802 CAPLUS
DN 133:293820
TI Differential distribution and defense involvement of antimicrobial peptides in mussel
AU **Mitta, Guillaume**; Vandenbulcke, Franck; **Noel, Thierry**; Romestand, Bernard; Beauvillain, Jean Claude; Salzet, Michel; **Roch, Philippe**
CS Laboratoire d'Endocrinologie des Annelides, Groupe de Neuroimmunite des Hirudinees, UPRES A 8017 CNRS, Universite des Sciences et Technologies de Lille, Villeneuve d'Ascq, 59655, Fr.
SO Journal of Cell Science (2000), 113(15), 2759-2769
CODEN: JNCSAI; ISSN: 0021-9533
PB Company of Biologists Ltd.
DT Journal
LA English
AB In previous papers, the authors characterized 3 types of 4-kDa, cysteine-rich, cationic antimicrobial peptides: MGDs (for Mytilus galloprovincialis defensins), mytilins and myticins, which are abundant in the mussel hemocytes. In the present work, the authors revealed a differential distribution of MGD1, mytilin B, and myticin B in cells of the digestive gland, gill, intestine, and adductor muscle sinus. In addn., using confocal and electron microscopy, the authors confirmed that defensins and mytilins were partially located in different subtypes of circulating hemocytes although the peptides can be located in the same cell, and even in the same granule. The authors also demonstrated that mytilins exert their microbiocidal effect within the cells through the process of phagosome-mytilin granule fusion leading to the co-location of ingested bacteria and mytilins.
RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:241254 BIOSIS
DN PREV200000241254
TI Mytilin B and MGD2, two antimicrobial peptides of marine mussels: Gene structure and expression analysis.
AU **Mitta, Guillaume**; **Hubert, Florence**; Dyrynda, Elisabeth A.; Boudry, Pierre; **Roch, Philippe (1)**
CS (1) UMR 219 Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER/CNRS Universite de Montpellier 2, Universite de Montpellier 2, CC 80, 34095, Montpellier France
SO Developmental & Comparative Immunology, (June, 2000) Vol. 24, No. 4, pp. 381-393.
ISSN: 0145-305X.
DT Article
LA English
SL English
AB Previous research has shown that mytilins and MGDs are two types of 4-kDa, cysteine-rich, cationic antimicrobial peptides, which are abundant in hemocytes of the mussels, Mytilus galloprovincialis and M. edulis. The expression of the genes encoding these peptides has been analyzed in the hemocytes of animals subjected to various stress factors, as well as during larval development. Variations in gene expression in adult mussels have been tested under conditions of physical stress, bacterial challenge and heat shock. The results suggest that in adult mussels, the MGD2 gene may be over-expressed with physical and temperature stress, but that reduced expression occurs with bacterial challenge. Gene expression during development has been analyzed using different larval and post-larval stages, ranging from 4-day-old veliger larvae to 32-day-old post-larvae.

Sciences et Techniques de Lille, Lille France
SO Developmental & Comparative Immunology, (2000) Vol. 24, No. Supplement 1, pp. S20. print.
Meeting Info.: 8th Congress of the International Society of Developmental and Comparative Immunology Cairns, Australia July 03-06, 2000
ISSN: 0145-305X.
DT Conference
LA English
SL English

L7 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3
AN 1999:483780 BIOSIS
DN PREV199900483780
TI **Myticin**, a novel cysteine-rich antimicrobial peptide isolated from haemocytes and plasma of the mussel Mytilus galloprovincialis.
AU **Mitta, Guillaume**; **Hubert, Florence**; **Noel, Thierry**; **Roch, Philippe (1)**
CS (1) UMR 219 DRIM, Universite de Montpellier 2, place Eugene Bataillon, F-34095, Montpellier France
SO European Journal of Biochemistry, (Oct., 1999) Vol. 265, No. 1, pp. 71-78.
ISSN: 0014-2956.
DT Article
LA English
SL English
AB We report here the isolation of two isoforms of a novel cysteine-rich peptide from haemocytes (isoform A of 4.438 Da and B of 4.562 Da) and plasma (isoform A) of the mussel, Mytilus galloprovincialis. The two molecules display antibacterial activity against gram-positive bacteria, whereas only isoform B is active against the fungus Fusarium oxysporum and a gram-negative bacteria Escherichia coli D31. Complete peptide sequences were determined by a combination of Edman degradation, mass spectrometry and cDNA cloning using a haemocyte cDNA library. The mature molecules, named myticins, comprise 40 residues with four intramolecular disulfide bridges and a cysteine array in the primary structure different to that of the previously characterized cysteine-rich antimicrobial peptides. Sequence analysis of the cloned cDNAs revealed that **myticin** precursors consist of 96 amino acids with a putative signal peptide of 20 amino acids, the antimicrobial peptide sequence and a 36-residue C-terminal extension. This structure suggests that myticins are synthesized as preproproteins and then processed by various proteolytic events before storage of the active peptide in the haemocytes. **Myticin** precursors are expressed mainly in the haemocytes as revealed by Northern blot analysis.

=> s l5 and antimicrobial peptide
L8 13 L5 AND ANTIMICROBIAL PEPTIDE

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9 8 DUP REM L8 (5 DUPLICATES REMOVED)

=> d bib ab 1-8

L9 ANSWER 1 OF 8 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT/ISI on STN
AN 2001-07093 BIOTECHDS
TI New **antimicrobial peptide** myticines obtainable from a bivalve mollusc, especially Mytilus galloprovincialis are useful for treatment and prevention of microbial disease;
useful as a antibiotic and fungicide in medicine, agriculture and aquaculture
AU Roch P; **Mitta G**; Hubert F; Noel T

AU **Mitta, Guillaume**; Vandenbulcke, Franck; **Noel, Thierry**; Romestand, Bernard; Beauvillain, Jean Claude; Salzet, Michel; **Roch, Philippe (1)**
CS (1) Defense et Resistance chez les Invertebres Marins (DRIM), IFREMER-CNRS-Universite de Montpellier 2, 34095, Montpellier France
SO Journal of Cell Science, (August, 2000) Vol. 113, No. 15, pp. 2759-2769. print.
ISSN: 0021-9533.
DT Article
LA English
SL English
AB In previous papers, we characterised 3 types of 4-kDa, cysteine-rich, cationic antimicrobial peptides: MGDs (for Mytilus galloprovincialis defensins), mytilins and myticins, which are abundant in the mussel hemocytes. In the present work, we revealed a differential distribution of the cells expressing the different genes. In addition, using confocal and electron microscopy, we confirmed that defensins and mytilins were partially located in different sub-types of circulating hemocytes although the peptides can be located in the same cell, and even in the same granule. We also demonstrated that mytilins exert their microbicidal effect within the cells through the process of phagosome-mytilin granule fusion leading to the co-location of ingested bacteria and mytilins.

L7 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 2
AN 2001100662 MEDLINE
DN 20570144 PubMed ID: 11119700
TI Original involvement of antimicrobial peptides in mussel innate immunity.
AU **Mitta G**; Vandenbulcke F; Roch P
CS Defense et Resistance chez les Invertebres Marins (DRIM), UMR 5098, Universite de Montpellier 2, France.
SO FEBS LETTERS, (2000 Dec 15) 486 (3) 185-90. Ref: 37
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200102
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201
AB Recently, the existence and extended diversity of antimicrobial peptides has been revealed in two mussel species. These molecules are classified into four groups according to common features of their primary structure: defensins, mytilins, myticins and mytimycin. In Mytilus galloprovincialis, gene structure reveals synthesis as precursors in circulating hemocytes. Synthesised even in absence of challenge, the precursors mature and the peptides are stored in granules as active forms. The different peptides are engaged in the destruction of bacteria inside phagocytes, before being released into hemolymph to participate in systemic responses. Such involvement in anti-infectious responses is unique, and apparently more related to those of mammalian phagocytes than to those of insects.

L7 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2000:377518 BIOSIS
DN PREV200000377518
TI A new model of involvement of antimicrobial peptides in invertebrates.
AU **Mitta, Guillaume (1)**; Vandenbulcke, Franck (1); Salzet, Michel (1); **Roch, Philippe**
CS (1) Centre de Biologie Cellulaire, Laboratoire d'Endocrinologie des Annelides, Groupe de Neuro-immunite des Hirudinees, Universite des